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EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/064,000	ELIA, JAMES P.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *382-394* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *382-394* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment filed 25 July 2005 and the supplemental amendment filed 02 August 2005 have been entered in full. The supplemental amendment of 02 August 2005 does not appear to be pertinent to the rejections of record. Since Applicant has not explained why the supplemental amendment should be considered pertinent to the rejections of record, the supplemental amendment will not be discussed further.

Claims 1-381 are canceled. Claims 382-394 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 382-388 under 35 U.S.C. § 112, first paragraph, as set forth at p. 9 of the previous Office Action (mailed 21 June 2005) is withdrawn upon further consideration.

35 U.S.C. § 112, Second Paragraph

Claims 383, 384, 391, 393, and 394 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis of this rejection is of record. Furthermore, new claims 391, 393, and 394 raise similar issues under 35 U.S.C. § 112, second paragraph. Claim 382 recites administration of cells. Claim 391

depends from claim 382 and further recites that the cells comprise pluripotent cells. Claim 393 depends from claim 391 and further recites that the cells are stem cells. Claim 394 depends from claim 393, and further recites that the stem cells are multifactorial and nonspecific. Regarding claims 391 and 393, it is implied that "stem cells" define a narrower sub-genus than "pluripotent cells." However, all pluripotent cells are stem cells. Neither the specification nor the art defines the terms so as to distinguish a difference between "pluripotent cells" and "stem cells." Thus, the metes and bounds of the two claims cannot be determined, and they are indefinite under 35 U.S.C. § 112, second paragraph. Also, claims 383 and 384 imply that "stem cells" defines a narrower sub-genus than "multifactorial and nonspecific cells," whereas claims 393 and 394 imply that "multifactorial and nonspecific cells" defines a narrower sub-genus than "stem cells." The two pairs of claims are contradictory. Since neither the specification nor the art provide a definition of "multifactorial and nonspecific cells," the metes and bounds of the claims cannot be determined, and they are indefinite under 35 U.S.C. § 112, second paragraph.

Applicant's arguments (pp. 7-11, amendment received 25 July 2005) have been fully considered but are not found to be persuasive for the following reasons.

Applicant argues that the examiner has proffered no sound reasoning in support of the conclusion that the description does not define the metes and bounds of the term "multifactorial and nonspecific cells." Applicant urges that the reasoning applied in the rejection under 35 U.S.C. § 102 which allegedly recognizes the ability of multifactorial and nonspecific cells to give rise to all of the cell types, appears to express an

understanding that is inconsistent with and contrary to the reasoning upon which the rejection under 35 U.S.C. § 112, second paragraph, was based. Applicant argues that the examiner's anticipation rejection was bottomed on an understanding of the multifactorial and nonspecific roles characteristic of pluripotent stem cells. Applicant concludes that the examiners' reasoning expressed in the anticipation rejection is correct, rendering any question of indefiniteness moot. This has been fully considered but is not found to be persuasive. The rejection of record is based on sound scientific reasoning, with referrals to the specification and definitions in the art as evidence in support of the rejection. See previous Office Action. Furthermore, examiners are instructed to examine each claim for compliance with each statute and rule, thereby avoiding piecemeal examination. See M.P.E.P § 704.01. Thus, while a claim may raise issues of indefiniteness necessitating a rejection under 35 U.S.C. § 112, second paragraph, the same claim still must be examined with respect to whether or not it reads on the prior art. In this situation, the M.P.E.P. instructs the examiner to give the claim its broadest reasonable interpretation, and apply art in rejections under 35 U.S.C. §§ 102 and 103 as appropriate. Therefore, both rejections under 35 U.S.C. §§ 112, second paragraph, and 102 are deemed appropriate.

Applicant argues that the examiner's statement regarding that stem cells are at least pluripotent "evinces a misunderstanding in regard to cell biology." Applicant asserts that not all stem cells are pluripotent, and that only non-specialized cells which possess the characteristics that enable such cells to be not fixed as to developmental potentialities are defined as pluripotent. Applicant concludes that those skilled in the art

understand well that all stem cells do not possess pluripotent characteristics. This has been fully considered but is not found to be persuasive because Applicant's characterization of stem cells is inconsistent with art-accepted definitions for such. Specifically, Stedman's Medical Dictionary (27th edition, 2000, Lippincott Williams and Wilkins) defines a stem cell as:

stem *c.* **1.** any precursor cell; **2.** a *c.* whose daughter *c.* may differentiate into other *c.* types.

It is noted that Applicant has relied upon no evidence to support their characterization of stem cells.

Applicant refers to p. 37, line 19 of the specification as defining "multifactorial and nonspecific cells" as stem cells and germinal cells. Applicant refers to p. 48, lines 13-15 as disclosing that, "if germinal cells (and in some cases, stem cells) are utilized a direct differentiation and morphogenesis into an organ can occur." Applicant argues that an organ is defined at p. 44, lines 12-18 of the specification as consisting "of two or more kinds of tissues joined into one structure that has a certain task." Applicant refers to p. 50, lines 2-5 as defining "multifactorial and nonspecific" growth factors as being "pluripotent." Applicant concludes that one skilled in the medical art, including declarants Drs. Heuser and Lorincz, based upon the above portions of the specification, would understand the meaning and intended scope of "multifactorial and nonspecific." This has been fully considered but is not found to be persuasive. Page 37, line 19, of the specification states, "Multifactorial and nonspecific cells (**such as** stem cells and germinal cells)..." (emphasis added). Such an exemplary list does not constitute a definition setting forth the metes and bounds of the phrase. The relevance of the quote from p. 44 is unclear. Page 50, lines 2-3, of the specification state, "The insertion of a

multifactorial and nonspecific growth factor (or gene) is required. Such a growth factor is pluripotent, senses what body part..." This section establishes that **one of the features** of a "multifactorial and nonspecific" growth factor (wherein a "growth factor" is defined in the specification as encompassing cells) is that it is pluripotent. This still does not constitute a definition setting forth the metes and bounds of the phrase. Stem cells are at least pluripotent. However, the specification does not limit the term "multifactorial and nonspecific" cells as being limited to stem cells. What cells other than stem cells can be considered to be "multifactorial and nonspecific?" Applicant's reference to declarants Drs. Heuser and Lorincz is not clear in this section of the arguments, since the arguments do not point to specific sections of specific declarations, and there are several declarations by Drs. Heuser and Lorincz.

Applicant takes issue with the examiner's statement that the disclosure at p. 37, line 19 does not constitute a definition setting forth the metes and bounds for the phrase multifactorial and nonspecific. Applicant argues that the examiner failed to specifically identify why the skilled artisan, based on the totality of the record, including Applicant's submissions and declaration evidence, would find Applicant's disclosure nondescriptive of the metes and bounds of the claimed invention. Applicant urges that there is no requirement to provide a definition for terms that are well known by those skilled in the art. This has been fully considered but is not found to be persuasive. Page 37, line 19 of the specification merely provides two examples of what is considered to be encompassed by the term "multifactorial and nonspecific cells." There is no other description of what features a multifactorial and nonspecific cell has. The art simply

does not use the term "multifactorial and nonspecific" with reference to cells. No evidence has been brought forth to challenge this statement. The examiner's search of the patent literature, non-patent literature, reference book literature (dictionaries, encyclopedias, etc.), and the internet has yielded no examples of the use of the term "multifactorial and nonspecific cell" by anyone other than Applicant. Each submission by Applicant, including declarations, has been carefully addressed on the record. In view of the totality of the evidence, the term "multifactorial and nonspecific cells" is determined to be indefinite. Perhaps most probative is consideration of the instant claims, which are self-contradictory regarding the metes and bounds of the term. Claims 383 and 384 imply that "stem cells" defines a narrower sub-genus than "multifactorial and nonspecific cells," whereas claims 393 and 394 imply that "multifactorial and nonspecific cells" defines a narrower sub-genus than "stem cells."

Applicant argues that it is clear from a reading of the specification that the qualities and characteristics of multifactorial and nonspecific cells can be found in pluripotent cells such as stem cells and germinal cells. Applicant urges that no one skilled in the art would seriously question that a fundamental property of all of these cells is that they are undifferentiated, or that "pluripotent" cells are undifferentiated stem cells which are highly versatile and can give rise to the growth of multiple tissues. Applicant argues that Dr. Elia recognized that such versatility results from their uniquely nonspecialized condition, which allows such cells to be used to carry out the nonspecific tissue function disclosed and claimed in the application for integrally growing soft tissue, including a new artery in a human patient. This has been fully considered but is not

found to be persuasive. This paragraph of Applicant's arguments does not clarify the differences between multifactorial and nonspecific cells, stem cells, pluripotent cells, and undifferentiated cells. The specification and the art also do not clearly define "multifactorial and nonspecific cells." Claims have been submitted that are directed to methods involving administration of cells, stem cells, pluripotent cells, and multifactorial and nonspecific cells, indicating that these types of cells are intended to define distinct cell populations. The claim dependencies specifically indicate that stem cells are a narrower sub-genus than multifactorial and nonspecific cells AND vice versa, which is contradictory. Therefore, the rejection under 35 U.S.C. § 112, second paragraph, is proper.

Applicant refers to Exhibit D of the Appeal Brief, indicating that it was cited to establish that the unique versatile and nonspecialized characteristics of pluripotent cells were known in the art. Applicant argues that the criticized language was employed to define a genus of cells that are characterized by having the capacity to promote the growth of all three major soft tissue types, i.e., pluripotent cells. This has been fully considered but is not found to be persuasive. Exhibit D uses the term "nonspecifically" to describe embryonic stem cells. Embryonic stem cells are omnipotent. Therefore, it is unclear whether "nonspecifically" means that the cells must be omnipotent or pluripotent. Also, the term "multifactorial" is not present in Exhibit D. Regarding Applicant's statement that pluripotent cells can promote the growth of all three major soft tissue types, this definition is also not consistent with the use of "pluripotent" by the

art. For example, Satoh et al. (2005, Leukemia (in press)) discusses myeloid-restricted hematopoietic stem cells and lymphoid-restricted hematopoietic stem cells (see Fig. 1).

Applicant argues that "multifactorial and nonspecific" is used to describe the pluripotent potentialities of stem cells and germinal cells. This is not found to be persuasive because Applicant now appears to be equating "multifactorial and nonspecific" with "puripotent." However, there are separate claims to methods of administering "multifactorial and nonspecific" cells and "pluripotent" cells. The claims imply that there is a difference between the terms; however, Applicant's arguments now appears to equate them.

Applicant indicates that the USPTO should take official notice that the term "pluripotent" is well known to those in the medical arts to describe versatile cells whose plasticity renders them capable of effecting growth of more than one type of tissue in the body. This has been fully considered but is not found to be persuasive. It is not clear why Applicant requires the USPTO to take official notice. Furthermore, Applicant's definition of "pluripotent" in the arguments was made without reference to the specification's definition, or a definition provided by the art.

Applicant argues that the skilled artisan would understand from the instant disclosure that multifactorial and nonspecific cells can be germinal cells or a stem cells. This has been fully considered but is not found to be persuasive because it adds nothing to the specification's exemplary list of cell types.

Applicant states that not all stem cells are multifactorial and nonspecific. This has been fully considered but is not found to be persuasive because it contradicts

Applicant's claims, definitions, and arguments. Claim 383 recites cells that are multifactorial and nonspecific. Claim 384, which depends from claim 383, recites that the multifactorial and nonspecific cells comprise stem cells. If claim 384 truly defines a narrower genus than claim 383, then it would seem that all stem cells are multifactorial and nonspecific, but not all multifactorial and nonspecific cells are stem cells. Thus, the arguments contradict the claims. The specification states, "Multifactorial and nonspecific cells (such as stem cells...)..." Such implies that all stem cells are multifactorial and nonspecific, in direct contradiction to Applicant's arguments. Applicant urges that multifactorial and nonspecific stem cells have the necessary plastic characteristics to promote growth of various types of soft tissue, including a new artery. Applicant refers to the examiner's question regarding what cells other than stem cells are multifactorial and nonspecific, arguing that the examiner answered the question by referring to p. 37 of the specification that multifactorial and nonspecific cells can include germinal cells in addition to stem cells. Applicant concludes that they are at a loss to understand why the examiner fails to comprehend that the subject specification sued such language to characterize a genus of cells that exhibit pluripotent characteristics. Applicant states that cells that do not exhibit such pluripotent characteristics cannot provide the integrated soft tissue growth required by the subject claims and are exclude from the scope of the claimed invention. This has been fully considered but is not found to be persuasive. Different claims are presented to administration of cells, stem cells, pluripotent cells, and "multifactorial and nonspecific" cells, thus implying that Applicant intended these terms to define distinct populations of cells. The specification states that

stem cells and germinal cells are examples of "multifactorial and nonspecific" cells, but fails to provide an exhaustive list of cells types or to otherwise characterize the features of the genus defined by the term. Applicant's arguments, which appear to equate the terms "multifactorial and nonspecific" with "pluripotent," do not serve to clarify the issue. Finally, the fact that the claim dependencies specifically indicate that stem cells are a narrower sub-genus than multifactorial and nonspecific cells (re: claims 383 and 384) AND vice versa (re: claims 393 and 394), is contradictory. In view of the totality of the evidence, the rejection under 35 U.S.C. § 112, second paragraph, is proper.

Applicant argues that they are not required to define well-known medical terminology that is readily understood by those in the art. Applicant refers to the second supplemental declarations of Drs. Heuser and Lorincz, at paragraphs 6 and 10, as evidence that the cellular growth factors described and claimed in the instant application are understood to include multifactorial and nonspecific cells. Applicant indicates that the examiner was in error to fail to weight the evidentiary value of these declarations. This has been fully considered but is not found to be persuasive, because there are no declarations of record in the instant application with the heading "second supplemental declaration." Since these declarations were submitted in related applications, Applicant may submit them in response to the instant office action, and they will be considered at that time.

Applicant summarizes that one skilled in the medical arts would understand that Applicant's description of multifactorial and nonspecific cells as including pluripotent stem cells and germinal cells is consistent with the knowledge of the art and would have

no difficulty in understanding the scope of protection sought by the claims. Applicant refers to p. 4 of the previous Office Action wherein the examiner acknowledges that one of the features of multifactorial and nonspecific growth factors (wherein a growth factor is defined in the specification as encompassing cells) is that it is pluripotent. Applicant submits that such descriptive language, when viewed by one skilled in the art, suffices to establish the scope of said term. Applicant argues that the purpose of 35 U.S.C. § 112 is to ensure due process of law, i.e., to give notice to the public as to the metes and boundaries adhering to patent claims. Applicant concludes that the rejection must fail for lack of a sound factual basis. This has been fully considered but is not found to be persuasive. Different claims are presented to administration of stem cells, pluripotent cells, and "multifactorial and nonspecific" cells, thus implying that Applicant intended these terms to define distinct populations of cells. The specification states that stem cells and germinal cells are examples of "multifactorial and nonspecific" cells, but fails to otherwise characterize the features of the genus defined by the term. Applicant's arguments, which appear to equate the terms "multifactorial and nonspecific" with "pluripotent," do not serve to clarify the issue. The fact that the claim dependencies specifically indicate that stem cells are a narrower sub-genus than multifactorial and nonspecific cells (re: claims 383 and 384) AND vice versa (re: claims 393 and 394), is contradictory. Regarding p. 4 of the previous Office Action, the examiner was quoting from the specification as follows. Page 50, lines 2-3 of the specification state, "The insertion of a multifactorial and nonspecific growth factor (or gene) is required. Such a growth factor is pluripotent, senses what body part..." This section establishes that **one**

of the features of a "multifactorial and nonspecific" growth factor (wherein a "growth factor" is defined in the specification as encompassing cells) is that it is pluripotent. This still does not constitute a definition setting forth the metes and bounds of the phrase. Stem cells and germinal cells are at least pluripotent. However, the term "multifactorial and nonspecific cells" is not clearly limited to stem cells. Applicant's repeated referral to stem cells and germinal cells as exemplary of "multifactorial and nonspecific" cells does not clarify the metes and bounds of "multifactorial and nonspecific" cells. In view of the totality of the evidence, the rejection under 35 U.S.C. § 112, second paragraph, is proper.

35 U.S.C. § 102

Claims 382-394 are rejected under 35 U.S.C. 102(b) as being anticipated by Lutjen et al., for the reasons set forth at pp. 7-8 of the previous Office Action (mailed 21 June 2005).

Applicant's arguments (pp. 13-18, amendment received 25 July 2005) have been fully considered but are not found t be persuasive for the following reasons.

Applicant provides remarks regarding "certain basic medical terminology" relating to cell biology, including definitions for totipotent, pluripotent, and unipotent stem cells. Applicant argues that the two-cell embryo of Lutjen et al. is totipotent, wherein totipotent cells are allegedly fixed as to developmental potentialities, i.e., the formation of a human being. Applicant argues that pluripotent cells do not have to ability to form a multicellular human being, and unipotent cells are capable of developing into only one

tissue type. Applicant urges that an understanding of these definitions should indicate that the rejection should be withdrawn. This has been fully considered but is not found to be persuasive. Applicant mischaracterizes the definitions at the referenced NIH website. The NIH's "Medline Plus" definitions for totipotent, pluripotent, and unipotent are in regard to cells in general, and NOT to stem cells. There is no such thing as a unipotent stem cell. If there were, then every dividing cell in an organism would be characterized as a stem cell, which is incorrect. Hepatocytes, for example, can divide to form daughter cells which are also hepatocytes. However, fully differentiated hepatocytes are not considered "stem cells." Also, while Applicant correctly copied the NIH's Medline Plus definition of "totipotent," Applicant's subsequent characterization of totipotent cells as having fixed developmental potentialities (i.e., the formation of a human being), is incorrect. The definition states that totipotent cells are capable of developing into a complete organism OR DIFFERENTIATING INTO ANY OF ITS CELLS OR TISSUES. For example, an embryonic stem cell, which is considered to be totipotent, can be induced to differentiate into neurons, which are useful in the treatment of various neurological diseases such as Parkinson's disease. See Fukuda et al., 2005, Expert Opin. Biol. Ther. 5. 5:1273-1280, especially, section 3, "Dopaminergic differentiation from embryonic stem cells."

Applicant implies that the examiner's use of the term "omnipotent" was incorrect since there is no definition for it in the above cited NIH Medline Plus dictionary website. Applicant posits that the examiner may have intended to use the term "totipotent." This has been fully considered but is not found to be persuasive, because others in the art

use the term "omnipotent stem cell." See Potter et al., 1999, Cell Tissue Res. 296 :235-246, abstract. However, it appears that "totipotent" and "omnipotent" can be considered synonyms with regard to stem cells.

Applicant refers to the examiner's query whether "nonspecific" means that a cell must be able to differentiate into any cell type or just more than one. Applicant states that a nonspecific cell has the potential to differentiate into multiple cell types and is not limited to a single cell type. This has been fully considered but is not found to be persuasive, because it does not clarify the issue. A totipotent stem cell has the potential to differentiate into any cell type. Since there are multiple cell types, a totipotent stem cell can also be said to have the potential to differentiate into multiple cell types.

Applicant argues that the examiner's statement that "all stem cells are at least pluripotent" is at variance with the NIH definitions provided because not all stem cells are pluripotent. Applicant argues that the language of the subject claims would be interpreted and understood by one skilled in the art by reading the specification and referring to the well-accepted and unambiguous terminology published by the NIH. Applicant states that their description of pluripotent cells in the specification is consistent with the definition published by the NIH. This has been fully considered but is not found to be persuasive. First, it bears repeating that the NIH definitions provided by Applicant did not characterize *stem* cells into three types, but rather characterized *any* cell as belonging to one of the three types. Stem cells are not unipotent; they are pluripotent and/or totipotent. It appears that Applicant considers the terms "totipotent" and "pluripotent" to be mutually exclusive, such that a totipotent cell would not also be

considered pluripotent. However, this is not true. The definition for pluripotent, provided by the NIH, is: "not fixed as to developmental potentialities." Such can also be said of a totipotent embryonic stem cell. In other words, totipotent cells can also be said to be pluripotent. (Of course, the reverse is not true. Not all pluripotent cells are also totipotent. For example, the myeloid-restricted hematopoietic stem cells of Satoh et al., *supra*, can form various myeloid cells, but not lymphoid cells. Such cells can be said to be pluripotent, but *not* totipotent.)

Applicant argues that claim 382 was amended to make explicit what was already implicit in the claim by adding that the grown soft tissue produced by the method of the invention is integrated into the body of the human patient, and that the produced and integrated soft tissue was at a selected site in the body of the patient, and the bud was formed at the selected site. Applicant argues that the amendment makes it clear that such growth and integration occurred in the previously claimed "in a body of a human patient" and not in a fetus that develops from an embryo. Applicant points to specific pages of the specification to support the new claim language. Applicant concludes that the additional claim language "integrating" and "selected site" removes any possible ambiguity as to where the bud and resultant soft tissue grow. This has been fully considered but is not found to be persuasive. Lutjen et al. teach a method for producing an integrating a desired soft tissue (an artery) at a selected site in a body of a human patient (in the uterus of a human patient) comprising placing cells (the embryo) in said body of said human patient (the uterus is in the body), forming a bud (such as a limb bud) at said selected site (inside the uterus) in said body of said human patient, and

growing and integrating said desired soft tissue (artery) in said body of said human patient from said bud. It is noted that a fetus is integrated into to body of a human patient. The claims do not require that the new artery must be formed outside the fetus that is integrated into the pregnant human patient's body. Lutjen et al. anticipates each limitation of each claim.

Applicant argues that the two-cell embryo utilized by Lutjen et al. is totipotent and, as such, can only result in formation of a multicellular human organism. Applicant reasons that the cells implanted by Lutjen and Applicant require distinct starting materials, which necessarily produce distinct end products. This has been fully considered but is not found to be persuasive. First, it is noted that none of the claims exclude totipotent cells. Claims 382, 385, 387, and 388 do not place limitations on the cells at all, and thus clearly encompasses totipotent cells. Claims 383, 384, 386, and 389-394 specify that the cells are multifactorial and nonspecific, and/or stem cells, and/or pluripotent. Given the indefiniteness of the term "multifactorial and nonspecific" as discussed above, the broadest reasonable interpretation of the claims encompasses the cells of Lutjen et al. Regarding "stem cells," it is noted that totipotent cells are stem cells. Regarding "pluripotent," it is noted that totipotent cells are also pluripotent. If a cell can develop into any differentiated cell type, it can also be said to be able to differentiate into more than one cell type. Finally, Applicant's statement that totipotent cells can only result in the formation of a multicellular human organism is incorrect with regard to the facts. Totipotent cells, such as embryonic stem cells, can be induced to differentiate into specific types of differentiated cells. See Fukuda et al. (2005, Expert

Opin. Biol. Ther. 5:1273-1280), who disclose that totipotent embryonic stem cells can be induced to differentiate into dopaminergic neurons.

Applicant urges that a two-cell embryo consists of totipotent cells, which are considered the "master cells" of the body because they contain all the genetic information needed to create all the cells of the human body plus the placenta, which nourishes the human embryo. Applicant argues that it is the ability to produce the placenta, which forms a barrier allowing only gas exchange between the developing conceptus and the human host that clearly distinguishes the two-cell embryo implanted by Lutjen et al. from the cells disclosed and claimed by Applicant. This has been fully considered but is not found to be persuasive. Again, Applicant is incorrect with regard to the facts. Almost all human cells having a nucleus and mitochondria contain all of the genetic information needed to create all the cells of the human body plus the placenta, because they all contain the identical genome. What determines whether a cell is a neuron or a keratinocyte or a hematopoietic cell or a totipotent stem cell or any cell type is the control of expression of the genome. See Alberts et al., eds., 1983, Molecular Biology of the Cell, Garland Publishing, Inc., New York, pp. 23-26. Applicant's characterization of a placenta is also incorrect, in that a placenta allows for more than just gas exchange between the mother and the fetus. See definition of a placenta from Stedman's Medical Dictionary (27th edition, 2000, Lippincort Williams and Wilkins), which states that a placenta allows for exchange of nutritive materials, waste materials, and even virus particles. Finally, since the claims do not require that the implanted cells be unable to form a placenta, Applicant's emphasis on the placenta is misplaced.

Applicant argues that the examiner's interpretation of the claims is unreasonable. Applicant refers to case law to support their assertion that the examiner must give the claims their broadest reasonable meaning in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise may be afforded by the written description contained in the applicant's specification. Applicant argues that the examiner has not pointed to a definition, specific disclosure, or any other pertinent information in the subject specification that either explicitly or implicitly teaches or infers that Applicant's alleged novel method of integrally growing soft tissue in a human patient encompasses implanting an embryo to grow a multicellular human organism. Applicant characterizes the invention as being directed to placing cells in the body of a human patient to grow soft tissue which integrates itself with the existing tissue in the patient. Applicant concludes that to continue to interpret the specification in the manner proposed by the examiner would be repugnant to such integrated tissue growth and would epitomize unreasonableness. Applicant indicates that that the claims must be interpreted in light of the specification, and the examiner should also interpret the amended and newly presented claims in such a manner. This has been fully considered but is not found to be persuasive. The examiner agrees that the claims must be given their broadest reasonable interpretation in light of the specification. However, case law also directs the examiner not to read limitations of the specification into the claims. See M.P.E.P. § 2111, which sets forth:

> Office personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). Limitations appearing in the specification but not recited in the claim are not read into the claim. > *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" without importing limitations from the specification into the claims unnecessarily).< *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.... An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.").

The meaning of the terms in the claims have been given their art-accepted meanings where such terms have art-accepted meanings. Indefinite terms have been given their broadest reasonable interpretation in light of the disclosure. None of the definitions in the instant specification or claims distinguish the claimed cells from the cells of Lutjen et al., as has been explained at great length on the record. Therefore, the rejection is reasonable.

Applicant argues that there exists a difference in kind between cells implanted by Applicant's invention, which result in growing and integrating soft tissue in the body of a human patient, and the embryo implanted in a human to accomplish *in vitro* fertilization for growing a multicellular human organism that ultimately develops into a separate functional entity. Applicant urges that because the potential of pluripotent cells is not total, such cells are not totipotent and are not embryos. Applicant concludes that to contend otherwise defies science as well as logic. This has been fully considered but is

not found to be persuasive. Lutjen et al. teach each method step of each claim in the instant application. Specifically, Lutjen et al. teach a method for producing an integrating a desired soft tissue (an artery) at a selected site in a body of a human patient (in the uterus of a human patient) comprising placing cells (the two-cell embryo) in said body of said human patient (the uterus is in the body), forming a bud (such as a limb bud) at said selected site (inside the uterus) in said body of said human patient, and growing and integrating said desired soft tissue (artery) in said body of said human patient from said bud. It is noted that a fetus, and all of its parts, are integrated into to body of a human patient. The claims do not require that the new artery must be formed outside the fetus that is integrated into the pregnant human patient's body. Lutjen et al. anticipates each limitation of each claim. Furthermore, claims 382, 385, 387, and 388 do not place limitations on the cells at all, and thus clearly encompasses the cells used by Lutjen et al. Claims 383, 384, 386, and 389-394 specify that the cells are multifactorial and nonspecific, and/or stem cells, and/or pluripotent. Given the indefiniteness of the term "multifactorial and nonspecific" as discussed above, the broadest reasonable interpretation of the claims encompasses the cells of Lutjen et al. Regarding "stem cells," it is noted that totipotent cells are stem cells. Regarding "pluripotent," it is noted that totipotent cells are also pluripotent. If a cell can develop into any differentiated cell type (totipotent), it can also be said to be able to differentiate into more than one cell type (pluripotent). Note that the definition of "pluripotent" given by the NIH website (and quoted by Applicant) states that the cells are not fixed as to developmental potentialities. It does not state that pluripotent cells are fixed to "some

but not all" developmental potentialities. As the skilled artisan is aware, all totipotent cells also meet the definition of pluripotent. Therefore, the rejection is reasonable, logical and scientifically correct.

Applicant characterizes claim 382 as explicitly requiring that the soft tissue grown from the bud is grown and integrated at a selected site in the human patient's body, and clearly defining allegedly novel subject matter by excluding the placenta-encased fetus resulting from embryo implantation of Lutjen et al. Applicant characterizes Lutjen et al. as embodying the development of a separate and ultimately independent multicellular human organism. Applicant states that it would be unreasonable and illogical to assert that the soft tissue of a developing fetus becomes integrated in the body of a host patient. Applicant characterizes claims 389-394 as further defining the allegedly novel subject matter by limiting the type of cells placed in the patient's body to form buds and limiting the type of soft tissue grown from such buds. Applicant concludes that claims 382-394 are novel. This has been fully considered but is not found to be persuasive. Claim 382 encompasses Lutjen et al.'s method of growing soft tissue (including an artery) from a bud (such as a limb bud) wherein the soft tissue is integrated (a fetus is integrated in the body of its mother) at a selected site (uterus) in the human patient's body. Claim 382 fails to define an invention that excludes the placenta-encased fetus resulting from embryo implantation of Lutjen et al., since the fetus is integrated into the body of its mother, and forms new arteries from a bud as a result of implantation of cells into the mother's uterus. Claims 383-394 also fail to distinguish the claimed invention

from the method of Lutjen et al. In view of the totality of the evidence and arguments, the rejection is reasonable and scientifically sound, and thus properly maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number

is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER